REMARKS

The specification has been amended to correct inadvertent typographical and grammatical errors, and the claims have been amended to clarify the invention. The specification has been amended at page 1, line 2 to recite the priority claim to PCT/US99/22685 as a continuation-in-part. The table at page 11, beginning at line 18 has been amended in column 1 to change SEQ ID NO:3 to SEQ ID NO:2. Support for this amendment is found in the specification, for example, at page 4, line 8 which describes SEQ ID NOs: 7 and 8 (column 2 of the table) as variants of SEQ ID NO:2. Claim 2 has been amended to delete SEQ ID NO:3 and to recite at 2b "the complement of SEQ ID NO:4-5". Claim 5 has been amended to recite a vector containing the polynucleotide "encoding SEQ ID NO:1". Claim 6 has been amended to recite an "isolated" host cell. Claim 7 has been amended at 7a to recite the protein of SEQ ID NO:1. Claim 11 has been amended to clarify the recited method, and claim 13 has been amended to recite the specific molecules or compounds listed in the alternative form. No new matter is added by any of these amendments, and entry of the amendments is therefore requested.

Claim Rejections Withdrawn

The Examiner stated the rejection of claims 1-13 under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific, substantial asserted utility or a well-established utility is withdrawn in light of applicants arguments. Further, the rejection of claims 1-13 under 35 U.S.C. 112, first paragraph, for lacking enablement is likewise withdrawn in light of applicants arguments.

New Grounds of Rejection

The Examiner stated that the disclosure is objected to for failing to state the relationship between the instant application and PCT/US99/22685 in the first line of the specification. Amendment of the specification to state that the instant application is a continuation or a continuation in part of said PCT is required.

The preliminary amendment filed May 24, 2001 claiming the benefit of the recited PCT application has been corrected herewith to specifically recite the instant application as a continuation in part of PCT/US99/22685. Withdrawal of the objection is therefore requested.

The Examiner also stated that the oath or declaration is defective. A new oath or declaration in compliance with CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because it fails to claim benefit to PCT/US99/22685 and U.S. provisional application 60/240,943.

A new declaration accompanies this response which includes the corrected priority claim, and withdrawal of the objection is therefore requested.

The Examiner stated that the specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Page 11, line 20 indicates that SEQ ID NO:3 and the variant SEQ ID NO:7 both products of claim 2, share sequence homology over residues 381 to 971. However, SEQ ID NO:3 consists of 276 residues in total and the sequence homology indicates an 82% identity over 591 residues. In the event that SEQ ID NO:3 were completely homologous across 276 residues of a 597 residue segment of SEQ ID NO:7 that would result in a sequence homology of 46.7%

Applicants have amended the table at page 11, beginning at line 18 to recite the full-length cDNA of SEQ ID NO:2 in column 1 (SEQ ID_H). SEQ ID NO:3, which is only a fragment of the full-length cDNA of SEQ ID NO:2, was mistakenly referenced in the table. SEQ ID NO:2 is the full-length human cDNA recited in the sequence listing as consisting of 1142 nucleotides. Nucleotides 381-971 recited in column 5 of the table at page 4 (Nt_H Alignment), recites the nucleotide sequence numbering of SEQ ID NO:2 over which the rat sequence (207717_Rn.2) was aligned. The value of 82% identity recited in column 4 of the table, therefore correctly reflects the results of the BLAST alignment for SEQ ID NO:2 against Incyte databases, conducted as described in the paragraph beginning at line 9 of page 11, and indicating the degree of sequence identity between the rat sequence over the recited range of 591 nucleotide residues of SEQ ID NO:2. The recited sequence identity between SEQ ID NO:7 and residues 381-971 of SEQ ID NO:2 is therefore correct. Withdrawal of the objection is therefore requested.

35 U.S.C. § 101, Rejection of Claim 6

The Examiner has rejected claim 6 under 35 U.S.C § 101 because the claimed invention is directed to non-statutory subject matter. Amendment to the claim to recite an isolated host cell would obviate this rejection. Claim 6 has been so amended, and withdrawal of the rejection is therefore requested.

35 U.S.C. § 112, Second Paragraph, Rejection of Claims 1-7, 11 and 13

The Examiner has rejected claims 1-7, 11 and 13 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner stated that claim 1 recites isolated cDNA comprising a nucleic acid sequence ... or a complement thereof. It is unclear if complement thereof refers to the nucleic acid sequence or the isolated cDNA. Dependent claims 4-13 are rendered vague and indefinite as it is unclear if they are limited to cDNA encoding the protein of claim 1, or if they embody the complement of said cDNA. For purposes of the examination, the Examiner stated, the claims will be read as encompassing both cDNA encoding a protein, and a complement.

Applicants point out that "the complement" of a cDNA of the Sequence Listing is defined in the specification at page 7, lines 11-13 as "a nucleic acid molecule which is completely complementary over its full length and which will hybridize to the cDNA ...". Thus, clearly the "complement thereof", as recited in claim 1, refers to an isolated cDNA that is the complete complement of the recited nucleic acid sequence. Claim 4 clearly recites a composition "comprising the cDNA or the complement of the cDNA of claim 1 ...". Claim 5 has been amended to recite only the polynucleotide encoding SEQ ID NO:1 (excluding the complement of said polynucleotide) and claims 6-7 are therefore also likewise limited. The remaining claims 8-13 reciting methods of detection and hybridization using the polynucleotides of claim 1 and 4 retain the use of both the recited cDNA or its complement. With these amendments and remarks, applicants believe the claims are clear and definite, and request withdrawal of the rejection of claims 1-7, 11 and 13 under 35 U.S.C. § 112, second paragraph.

The Examiner stated that claim 2a recites "a fragment of SEQ ID NO:2 selected from SEQ ID NO:3-5 or the complement thereof". It is unclear if complements thereof refers to SEQ

ID NO:3-5 or fragments of SEQ ID NO:2.

Claim 2b has been amended to specifically recite "the complement of SEQ ID NO:4-5".

The Examiner stated that claim 7 recites a method comprising culturing a host cell of claim 6 under conditions for protein expression and recovering the protein. However, it is unclear that the protein encoded by the cDNA of claim 1 is recovered from the culture. Host cells express many proteins which are endogenous to the cell itself, therefore without a limitation such as a statement that the recovered protein is the protein encoded by SEQ ID NO:2, it is unclear what protein is being produced.

Claim 7 has been amended at 7b to recite the protein of SEQ ID NO:1 produced by the claimed method.

The Examiner stated that claim 11 is drawn to a method of using a cDNA to detect expression of a nucleic acid in a sample comprising hybridizing the composition of claim 4 to a nucleic acid sample under conditions to form at least one hybridization complex; and detecting hybridization complex formation, wherein complex formation indicates expression of the nucleic acid in the sample, wherein the cDNA is differentially expressed when compared with a standard and (is) diagnostic of colon cancer or colon polyps. The Examiner stated that the method is vague and indefinite in that there is no definition or limitation for "a standard"; and there is no active method step linking the outcome of comparison with said standard to the diagnosis of colon cancer or colon polyps.

Applicants submit that the meaning of "a standard" as used in the context of the claim is readily understood by one of skill in the art based on the specification and the knowledge of one skilled in the art. In particular, in describing the use of the claimed method for measuring differential expression in a biological sample compared to "a standard" to determine the presence of a disorder, the specification recites at page 18:

> In order to provide standards for establishing differential expression, normal and disease expression profiles are established. This is accomplished by combining a sample taken from normal subjects, either animal or human, with a cDNA under conditions for hybridization to occur. Standard hybridization complexes may be quantified by comparing the values obtained using normal subjects with values from an experiment in which a known amount of a purified sequence is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who were diagnosed with a particular condition, disease, or disorder. Deviation from standard values toward those

associated with a particular disorder is used to diagnose that disorder. (Emphasis added)

Thus, the skilled artisan would clearly understand that "a standard" as used in the context of claim 11 would pertain to a predetermined level of expression of the nucleic acid in question in normal tissue as the "standard" to which comparison in the subject sample is made. Differential expression (defined as at least two-fold; specification at page 7) between the subject sample and the standard would then be indicative of the presence of the disorder. With regard to the Examiner's allegation that there is not a proper "linking step" with the outcome of the comparison and the disease diagnosis, applicants have amended the claim to recite " ... and wherein the differential expression is diagnostic of a colon cancer or colon polyps in the sample". Applicants submit that this amendment makes it clear that the "outcome of the comparison" is the differential expression observed between the subject sample and the standard, and that it is this differential expression that is linked with the presence of the disorder, i.e., colon cancer or colon polyps.

The Examiner stated that claim 13 recites an improper Markush Group and advised applicants to read ---peptides or transcription factors---. Claim 13 has been so amended.

With these amendments and remarks, applicants submit that claims 1-7, 11 and 13 are clear and definite, and therefore request withdrawal of the rejection of these claims under 35 U.S.C. § 112, second paragraph.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 2 and 7-13

The Examiner has rejected claims 2 and 7-13 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to reasonably to convey to one skill in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(A) As drawn to polynucleotides comprising ESTs

The Examiner stated that claim 2 is drawn to an isolated cDNA comprising SEQ ID NO:3-5 or the complement of SEQ ID NO:3-5. SEQ ID NO:3-5 are partial DNA sequences ... of SEQ ID NO:2. Claim 2 is therefore drawn to a genus of nucleic acids in that it encompasses any nucleic sequence that minimally comprises SEQ ID NO:3-5 within it, including any full gene which contains the sequence, and any fusion constructs. Therefore when given the broadest

reasonable interpretation, the claim encompasses full length genes that are not fully described. The Examiner suggested that amendment of the claim drawn to SEQ ID NO:3-5 to nucleic acids consisting of rather than comprising, would obviated this rejection. Claim 2 has been so amended at 2b.

(B) As drawn to a method for using a cDNA to produce a protein, wherein said protein is the complementary sequence of SEQ ID NO:2, and is drawn to methods of using a cDNA to detect expression of a nucleic acid, wherein the cDNA is not the complementary sequence to SEQ ID NO:2.

The Examiner stated that claim 8 is drawn to a method for using a cDNA to detect expression of a nucleic acid in a sample comprising hybridizing the composition of claim 4 to nucleic acid of the sample. Claim 4 clearly encompasses both the cDNA of claim 1 and the complement of the isolated cDNA. Claim 7 is drawn to a method of using a cDNA to produce a protein wherein the cDNA encoding SEQ ID NO:1 or the complement of said cDNA is used to produce the protein. Claims 7-11 depend on a genus of expressed nucleic acids encompassing nucleic acids which encode intelectin and nucleic acids which encode a completely unrelated protein. The specification teaches a method of using the complementary nucleic acid to the nucleic acids which encode SEQ ID NO:1 for the detection of the nucleic acids encoding intelectin within the sample. Since the claims depend upon a protein yet to be discovered, i.e., the translated product of the sequence which hybridizes to the nucleic acids encoding SEQ ID NO:1, the disclosure is insufficient to describe the genus.

Applicants' Response

The amendment to claim 5 excluding the "complement" of the nucleic acid encoding SEQ ID NO:1 has been discussed supra. Claim 7 is therefore now limited to a method of using a cDNA to produce a protein of SEQ ID NO:1 only. Claims 8-11, however, retain the use of either the cDNA encoding SEQ ID NO:1 or its complement in methods to detect expression of a nucleic acid in a sample because of the well known fact that most nucleic acids exist in their natural state in a double-stranded form. Therefore, the use of the cDNA encoding SEQ ID NO:1 or its complement in these methods is readily apparent to one skilled in the art independent of any protein that may or may not be encoded by the complementary polynucleotide.

(C) As drawn to a method of using a cDNA to screen a plurality of molecules which specifically

bind the cDNA (peptides, transcription factors).

The Examiner stated that claim 12 is drawn to a method for using a cDNA to screen a plurality of molecules or compounds to identify a molecule or compound that specifically binds to the cDNA, and claim 13 embodies specific categories of molecules or compounds to be screened by the method. The Examiner stated that there are no structural or functional restrictions on the plurality of molecules or compounds used in the method. The specification discloses complementary nucleic acid sequences which will specifically bind to the expressed nucleic acid sequence of SEQ ID NO:1 (sic, SEQ ID NO:2) or which encode SEQ ID NO:1. Thus, the Examiner stated, the disclosure adequately describes the genus of nucleic acid molecules encompassing RNA, DNA, peptide nucleic acid and artificial chromosomal constructs. However, the genus of molecules or compounds includes peptides and transcription factors, and the disclosure does not anticipate the structural or functional features of peptides and transcription factors.

Applicants' Response

The specification adequately describes the meaning of "specific binding" at page 9, lines 12-15 of the specification, and also provides a representative method of measuring specific binding to the claimed cDNAs or protein at page 36, Example XV. Since the clear purpose of the claimed method is to identify molecules or compounds that will specifically bind the claimed polynucleotides, it is not necessary to "predetermine" what structural or functional features the candidate molecules or compounds must possess in order to practice the claimed method. Since it is the method of screening candidate molecules or compounds for specific binding to the claimed polynucleotides that is claimed, and not the candidate molecules themselves, one skilled in the art would readily recognize applicants possession of the method of screening based on the disclosure in the specification.

With these amendments and remarks, applicants believe that one skilled in the art would readily recognize applicants possession of the claimed invention, at least as recited in claims 2 and 7-13, and therefore request withdrawal of the rejection of these claims under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 4 and 8-11

The Examiner has rejected claims 4 and 8-11 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for detecting expressed nucleic acid SEQ ID NO:2 or the nucleic acid encoding SEQ ID NO:1, does not reasonably provide enablement for the detection of the nucleic acids comprising the complement of SEQ ID NO:2 or the complement of the nucleic acids encoding SEQ ID NO:1. The Examiner stated that claim 8 is drawn in part to a method of using the nucleic acid encoding SEQ ID NO:1 for the detection of expression of nucleic acids within a sample. For the reasons stated above, sequence(s) which are complementary to SEQ ID NO:2 or the nucleic acids encoding SEQ ID NO:1 would not be expected to encode intelectin or a protein similar to intelectin.

Applicants' Response

As stated above, in response to the previous rejection of claim 8 in part (B), the use of the recited polynucleotide or its complement in methods of nucleic acid detection is not dependent on any protein which may or may not be encoded by the complement of SEQ ID NO:2 or of any other polynucleotide encoding SEQ ID NO:1. Because of the double-stranded nature of native nucleic acids, the presence of SEQ ID NO:2, for example, or its complete complement, in a sample is indicative of the presence of SEQ ID NO:2 itself in the sample, and therefore the use of the complementary strand or the sequence itself in the disclosed method of detection is clearly enabled by the specification. Withdrawal of the rejection of claim 8 under 35 U.S.C. § 112, first pargraph is therefore requested.

35 U.S.C. § 102(e), Rejection of Claims 1, 2, 4-10, 12 and 13

The Examiner has rejected claims 1, 2, 4-10, 12 and 13 under 35 U.S.C. § 102(e) as being anticipated by Pierce et al. (U.S. 6,146,849). Pierce et al. disclose the cDNA clone of HL-13 (SEQ ID NO:5) which encodes an amino acid sequence identical to the instant SEQ ID NO:1 with the exception of an arginine residue at position 103. The Examiner stated that since the specification defines "complement" on page 7, lines 11-13 as a nucleic acid sequence which will hybridize to cDNA or mRNA under conditions of high stringency, the complement of the cDNA disclosed by Pierce et al. would hybridize under stringent conditions to the instant SEQ ID NO:2 because there is only one nucleotide difference out of 975 nucleotides of the coding region.

Further, the Examiner stated, the instant SEQ ID NO:3-5 would hybridize to the complement of the coding region of the Pierce SEQ ID NO:5 as there would be no mismatched nucleotides for SEQ ID NO:3 and only a single mismatched nucleotide for SEQ ID NO:4 and 5.

Applicants' Response

Claim 2 has been amended to delete SEQ ID NO:3. As discussed previously, the full definition of "the complement" given at page 7 of the specification recites "... a nucleic acid molecule which is completely complementary over its full length and which will hybridize to the cDNA or an mRNA under conditions of high stringency" (emphasis added). Thus, the limiting parameter of the definition is that "the complement" of a recited sequence of the Sequence Listing must be identical in its complementary base pair at every nucleotide position over the full length of the complementary nucleic acid sequence in addition to its ability to hybridize under high stringency conditions to the target sequence. Claims 1 and 2 recite "An isolated cDNA comprising a nucleic acid sequence ... or the complement thereof ...". Said complementary sequence must therefore be identical in complementarity over its full length and to the full length of the recited SEQ ID NO:. Pierce et al do not disclose a sequence which is the complete complement of SEQ ID NO:2, 4 or 5 of the instant invention, and applicants therefore request withdrawal of the rejection of claims 1, 2, 4-10, 12 and 13 under 35 U.S.C. § 102(e) as being anticipated by Pierce et al.

35 U.S.C. § 102(b), Rejection of Claims 1 and 2

The Examiner has rejected claims 1 and 2 under 35 U.S.C. § 102(b) as being anticipated by the New Englands Biolab Catalog (1993-1994, page 91). The New Englands Biolab Catalog discloses random hexamers which will be complementary across their full length to the nucleic acids encoding SEQ ID NO:1 and SEQ ID NO:2-5.

Applicants arguments regarding the definition of "the complement thereof" as recited in claims 1 and 2 above are referenced herein. The random hexamers recited in the New Englands Biolab Catalog do not anticipate a nucleic acid sequence which the complete complement of SEQ ID NO:2, 4 or 5, or of a nucleic acid sequence encoding SEQ ID NO:1. Withdrawal of the rejection of claims 1 and 2 as anticipated by New Englands Biolab Catalog is therefore requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE CORPORATION

Date: June 11, 2003

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Docket No.: PC-0027 US

Applicants: Yue et al.
Serial No.: 09/771,503
Filing Date: January 26, 2001
Title: INTELECTIN

Enclosed:

1. Return Receipt Postcard;
2. Transmittal Fee Sheet (1 pg., in duplicate);
3. Response to Office Action (14 pp.); and
4. Supplemental Declaration and Power of Attorney (12 pp., signed in counter-part).

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